

DECLARATION UNDER RULE 132	Application #	10/587,899
	Confirmation #	8912
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	First Inventor	SCHWARTZ Jean-Charles
	Art Unit	1614
	Examiner	Spivack, Phyllis G.
	Docket #	P08977US00/BAS

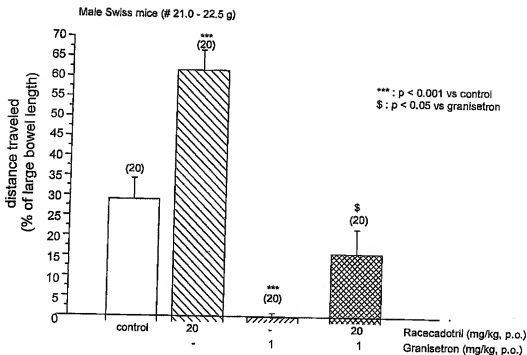
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

S I R:

I, Jeanne-Marie Lecomte, residing in Paris (75003), 30 rue des Francs-Bourgeois, France, declare and say as:

1. I am a French citizen.
2. I am Ph.D in Sciences, author of more than 120 scientific publications in different fields, including clinical pharmacology and clinical trials, and presently Chairman of Bioprojet.
3. I am aware that the instant claims are being rejected under 35 USC103(a) as being unpatentable over Stroppolo et al, in view of Boige et al.
4. Nevertheless, none of the above references suggests the synergy which we surprisingly found when combining racecadotril and ondansetron.
5. Racecadotril or dexecadotril exhibit an anti-secretory effect in that they inhibit associated loss of water in diarrheic patients. Loss of water is one of the main complications in diarrhoea. However, these agents may induce an increase in the intestinal transit. This increase is a possible undesirable side effect of racecadotril. We surprisingly showed that coadministration of racecadotril or granisetron suppresses the increase in the intestinal transit induced by racecadotril while maintaining the anti-secretory activity.
6. The following data show the effect of racecadotril alone or together with granisetron on the transit of a charcoal meal in the large bowel in fasted male Swiss mice.





The above scheme shows, more precisely, that co-administration of racecadotril with granisetron suppresses the side effects of racecadotril. This could not have been expected by the skilled person. The combinations of an anti-emetic agent with an enkephalinase inhibitor thus involves an inventive step.

7. The undersigned declares further that all statements made herein of his knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that wilful false statements and the like so made are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of United States Code and that such wilful false statements may jeopardize the validity of the application or any patent issuing thereon.

Signed this 26th day of February 2009

Jeanne-Marie LECOMTE